MECP2-related severe neonatal encephalopathy

MECP2-related severe neonatal encephalopathy is a neurological disorder that primarily affects males and causes brain dysfunction (encephalopathy). Affected males have a small head size (microcephaly), poor muscle tone (hypotonia) in infancy, movement disorders, rigidity, and seizures. Infants with this condition appear normal at birth but then develop severe encephalopathy within the first week of life. These babies experience poor feeding, leading to a failure to gain weight and grow at the expected rate (failure to thrive). Individuals with *MECP2*-related severe neonatal encephalopathy have severe to profound intellectual disability. Affected males have breathing problems, with some having episodes in which breathing slows or stops for short periods (apnea). As the child ages, the apnea episodes tend to last longer, especially during sleep, and affected babies often require use of a machine to help regulate their breathing (mechanical ventilation). Most males with *MECP2*-related severe neonatal encephalopathy do not live past the age of 2 because of respiratory failure.

MECP2-related severe neonatal encephalopathy is the most severe condition in a spectrum of disorders with the same genetic cause. The mildest is PPM-X syndrome, followed by *MECP2* duplication syndrome, then Rett syndrome (which exclusively affects females), and finally *MECP2*-related severe neonatal encephalopathy.

Frequency

MECP2-related severe neonatal encephalopathy is likely a rare condition. Twenty to 30 affected males have been reported in the scientific literature.

Genetic Changes

Mutations in the *MECP2* gene cause *MECP2*-related severe neonatal encephalopathy. The *MECP2* gene provides instructions for making a protein called MeCP2 that is critical for normal brain function. Researchers believe that this protein has several functions, including regulating other genes in the brain by switching them on or off as they are needed. The MeCP2 protein likely plays a role in maintaining the normal function of nerve cells, which ensures that connections (synapses) between these cells form properly. The MeCP2 protein may also control the production of different versions of certain proteins in nerve cells. Although mutations in the *MECP2* gene disrupt the normal function of nerve cells, it is unclear how these mutations lead to the signs and symptoms of *MECP2*-related severe neonatal encephalopathy.

Inheritance Pattern

MECP2-related severe neonatal encephalopathy has an X-linked pattern of inheritance. A condition is considered X-linked if the mutated gene that causes the disorder is located on the X chromosome, one of the two sex chromosomes in each cell. In males, who have only one X chromosome, a mutation in the only copy of the gene in each cell is sufficient to cause the condition. In females, who have two X chromosomes, a mutation in one of the two copies of the gene in each cell is usually sufficient to cause the condition. However, females with a mutation in the *MECP2* gene do not develop *MECP2*-related severe neonatal encephalopathy. Instead, they typically develop Rett syndrome, which has signs and symptoms that include intellectual disability, seizures, and movement problems.

In some cases, males with *MECP2*-related severe neonatal encephalopathy inherit the mutation from a mother with mild neurological problems or from a mother with no features related to the mutation. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons. Other cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

Other Names for This Condition

- methyl-cytosine phosphate guanine binding protein 2 related severe neonatal encephalopathy
- severe congenital encephalopathy due to MECP2 mutation
- severe neonatal encephalopathy due to MECP2 mutations

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Severe neonatal-onset encephalopathy with microcephaly
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1968556/

Other Diagnosis and Management Resources

- GeneReview: MECP2-Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1497
- Johns Hopkins Children's Center: Failure to Thrive
  http://www.hopkinsmedicine.org/healthlibrary/conditions/adult/pediatrics/failure_to_thrive_90,p02297/

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html
- Health Topic: Respiratory Failure
  https://medlineplus.gov/respiratoryfailure.html

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Encephalopathy Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Encephalopathy-Information-Page
- National Institute of Neurological Disorders and Stroke: Microcephaly Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Microcephaly-Information-Page

Educational Resources

- Boston Children's Hospital: Seizures
  http://www.childrenshospital.org/conditions-and-treatments/conditions/seizures
- Centers for Disease Control and Prevention: Intellectual Disability
  https://www.cdc.gov/ncbddd/actearly/pdf/parents_pdfs/IntellectualDisability.pdf
- Cleveland Clinic: Microcephaly in Children
  http://my.clevelandclinic.org/childrens-hospital/health-info/diseases-conditions/hic-Microcephaly
- Cleveland Clinic: Sleep Apnea
  http://my.clevelandclinic.org/health/articles/sleep-apnea

- Disease InfoSearch: Encephalopathy, neonatal severe, due to MECP2 mutations
  http://www.diseaseinfosearch.org/Encephalopathy%2C+neonatal+severe%2C+due+to+MECP2+mutations/8310
- Johns Hopkins Children's Center: Failure to Thrive
  http://www.hopkinsmedicine.org/healthlibrary/conditions/adult/pediatrics/failure_to_thrive_90,p02297/
- Kennedy Krieger Institute: Epilepsy (Seizure Disorder)
  https://www.kennedykrieger.org/patient-care/diagnoses-disorders/epilepsy-seizure-disorder
- Kennedy Krieger Institute: Intellectual Disability
  https://www.kennedykrieger.org/patient-care/diagnoses-disorders/intellectual-disability
- MalaCards: mecp2-related severe neonatal encephalopathy
  http://www.malacards.org/card/mecp2_related_severe_neonatal_encephalopathy
- Orphanet: Severe neonatal-onset encephalopathy with microcephaly
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=209370

Patient Support and Advocacy Resources

- Rare Disease Clinical Research Network: Rett Syndrome, MECP2 Duplication and Rett-Related Disorders Natural History Study
  https://www.rarediseasesnetwork.org/cms/rett/Get-Involved/Studies/5211
- RettSyndrome.org
  https://www.rettsyndrome.org/

GeneReviews

- MECP2-Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1497

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28mecp2-related+severe+neonatal+encephalopathy%29+OR+%28severe+neonatal+encephalopathy%29+AND+%28mecp2%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

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